

Applicants : BERMUDEZ, et al.  
U.S. Serial No.: 10/790,586  
Filed : March 1, 2004  
Page : 3

Amendments to the claims:

Please cancel claims 1-9 and 11-18 without prejudice to the Applicants' rights to pursue the subject matters in a future application, and add new claims 25-43.

1. (Canceled) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and an attenuated, tumor-targeting Gram-negative bacterium containing a bacteriophage, wherein the genome of the bacteriophage has been modified to encode for a gene product of interest under the control of an eukaryotic promoter or wherein the genome of the bacteriophage has been modified to encode the gene of interest as a fusion protein with a bacteriophage capsid protein.

2. (Canceled) The composition according to claim 1 in which the bacterium is a *Salmonella*.

3. (Canceled) The composition according to claim 1 in which the Gram-negative bacterium is *Shigella*.

4. (Canceled) The composition according to claim 1 in which the gene product of interest is a proteinaceous molecule.

5. (Canceled) The composition according to claim 1 in which the gene product of interest is an antigen.

6. (Canceled) The composition according to claim 4 in which the molecule is selected from the group consisting of a

**Applicants** : **BERMUDES, et al.**  
**U.S. Serial No.:** **10/790,586**  
**Filed** : **March 1, 2004**  
**Page** : **4**

cytokine, a cytotoxin, a pro-drug converting enzyme and an anti-angiogenic agent.

7. (Canceled) The composition according to claim 6 in which the cytotoxin is a bacteriocin.

8. (Canceled) A kit comprising an attenuated, tumor-targeting Gram-negative bacterium containing a bacteriophage, wherein the genome of the bacteriophage has been modified to encode for a gene product of interest under the control of an eukaryotic promoter or wherein the genome of the bacteriophage has been modified to encode the gene of interest as a fusion protein with a bacteriophage capsid protein, together with instructions for administering the attenuated, tumor-targeting Gram-negative bacterium containing a bacteriophage to a subject to deliver the gene product of interest.

9. (Canceled) A kit comprising an attenuated, tumor-targeting Gram-negative bacterium expressing the F' pilus and a filamentous bacteriophage, wherein the genome of the bacteriophage has been modified to encode for a gene product of interest under the control of an eukaryotic promoter or wherein the genome of the bacteriophage has been modified to encode the gene of interest as a fusion protein with a bacteriophage capsid protein, together with instructions for administering the attenuated, tumor-targeting Gram-negative bacterium expressing the F' pilus and a filamentous bacteriophage to a subject to deliver the gene product of interest.

**Applicants** : **BERMUDES, et al.**  
**U.S. Serial No.:** **10/790,586**  
**Filed** : **March 1, 2004**  
**Page** : **5**

10. (Canceled)

11. (Canceled) A method for delivering an agent comprising administering, to a subject, a pharmaceutical composition comprising an attenuated Gram-negative bacterium containing a bacteriophage, wherein the bacteriophage genome has been modified to encode for a gene product of interest under the control of an eukaryotic promoter or wherein the genome of the bacteriophage has been modified to encode for a gene of interest as a fusion protein with a bacteriophage capsid protein.

12. (Canceled) The method according to claim 11, in which the gene of interest is an antigen or a pro-drug converting enzyme.

13. (Canceled) The method according to claim 11, in which the gene of interest is fused with a bacteriophage capsid protein.

14. (Canceled) A method for delivering an agent comprising administering, to a subject, a pharmaceutical composition comprising an attenuated Gram-negative bacterium expressing the F' pilus and a filamentous bacteriophage, wherein the bacteriophage genome has been modified to encode for a gene product of interest under the control of an eukaryotic promoter or wherein the genome of the bacteriophage has been modified to encode for a gene of interest as a fusion protein with a bacteriophage capsid protein.

Applicants : BERMUDEZ, et al.  
U.S. Serial No.: 10/790,586  
Filed : March 1, 2004  
Page : 6

15. (Canceled) A method of inhibiting tumor growth or reducing tumor volume comprising administering, to a subject in need of such inhibition or reduction, a pharmaceutical composition comprising an attenuated, tumor-targeting Gram-negative bacterium containing a bacteriophage, wherein the bacteriophage genome has been modified to encode for a gene product of interest under the control of an eukaryotic promoter or wherein the genome of the bacteriophage has been modified to encode the gene of interest as a fusion protein with a bacteriophage capsid protein.

16. (Canceled) The method according to claim 15 in which the Gram-negative bacterium is *Salmonella* or *Shigella*.

17. (Canceled) A method of inhibiting tumor growth or reducing tumor volume comprising administering, to a subject in need of such inhibition or reduction, a pharmaceutical composition comprising an attenuated, tumor-targeting Gram-negative bacterium expressing the F' pilus and a bacteriophage, wherein the bacteriophage genome has been modified to encode for a gene product of interest under the control of an eukaryotic promoter or wherein the genome of the bacteriophage has been modified to encode the gene of interest as a fusion protein with a bacteriophage capsid protein.

18. (Canceled) The method according to claim 17 in which the Gram-negative bacterium is *Salmonella* or *Shigella*.

Applicants : BERMUDEZ, et al.  
U.S. Serial No.: 10/790,586  
Filed : March 1, 2004  
Page : 7

19.-24. (Canceled)

**Please add the following new claims 25-43, as follows:**

25. A Salmonella strain which expresses F' pilus and produces filamentous bacteriophage and is capable of targeting tumors by intravenous administration.

26. A Salmonella strain which expresses F' pilus and produces filamentous bacteriophage and is capable of targeting tumors by intravenous administration and producing phage directly within tumors.

27. (New) The Salmonella according to Claim 25, wherein the Salmonella is attenuated.

28. (New) The Salmonella according to Claim 26, wherein the Salmonella is attenuated.

29. (New) A composition comprising the Salmonella of claim 25.

30. (New) A composition comprising the Salmonella of claim 26.

31. (New) The composition according to Claim 29, wherein the Salmonella is attenuated.

**Applicants** : **BERMUDES, et al.**  
**U.S. Serial No.:** **10/790,586**  
**Filed** : **March 1, 2004**  
**Page** : **8**

32. (New) The composition according to Claim 30, wherein the Salmonella is attenuated.

33. (New) The composition according to Claim 31 in which the Salmonella strain is attenuated by an msbB- mutation.

34. (New) The composition according to Claim 31 in which the Salmonella is attenuated by a pur- mutation.

35. (New) The composition according to Claim 32 in which the Salmonella strain is attenuated by an msbB- mutation.

36. (New) The composition according to Claim 32 in which the Salmonella is attenuated by a pur- mutation.

37. (New) A method for delivering filamentous bacteriophage to solid tumors by intravenous administration of attenuated tumor-targeted Salmonella engineered to contain a filamentous bacteriophage of interest.

38. (New) A kit comprising an attenuated, tumor-targeting Salmonella expressing F' pilus suitable for delivery of a filamentous bacteriophage cloning vector to tumors by intravenous administration.

39. (New) A kit according to claim 38 in which the filamentous bacteriophage cloning vector possesses a eukaryotic promoter.

Applicants : BERMUDEZ, et al.  
U.S. Serial No.: 10/790,586  
Filed : March 1, 2004  
Page : 9

40. (New) The Salmonella according to claim 25, wherein the Salmonella is capable of delivering between  $2.7 \times 10^9$  p.f.u. (plaque forming unit)/gram and  $4.6 \times 10^{11}$  p.f.u./gram of phage to tumors.

41. (New) The Salmonella according to claim 26, wherein the Salmonella is capable of delivering between  $2.7 \times 10^9$  gram p.f.u./gram and  $4.6 \times 10^{11}$  p.f.u./gram of phage to tumors.

42. (New) The Salmonella according to claim 27, wherein the Salmonella is capable of delivering between  $2.7 \times 10^9$  p.f.u./gram and  $5.9 \times 10^9$  p.f.u./gram of phage to tumors.

43. (New) The Salmonella according to claim 28, wherein the Salmonella is capable of delivering between  $2.7 \times 10^9$  p.f.u./gram and  $5.9 \times 10^9$  p.f.u./gram of phage to tumors.